## REMARKS

Claims 1-10, 14-52, 58-60 and 65-68 are pending in this application. Claims 1-10 and 14-52 are withdrawn from consideration. Claims 11-13, 53-57 and 69-72 have been cancelled. Claims 58-60 and 65-68 have been rejected under 35 U.S.C. § 102(e).

Amendments to the Specification

The Applicants amend the first paragraph following the title to state priority to the earlier PCT application, which itself claims priority to an earlier British application. Priority was earlier claimed by filing copies of the British and PCT applications on September 24, 2004.

## Anticipation

First, "a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987).

The Morris reference having the text copy of the file provided with the latest Office Action, does not anticipate the claims because it fails to disclose a portion of a full-length sequence as recited in the claims. Instead, Morris merely discloses a partial amino acid sequence comprising the first 85 amino acids of SEQ ID NO: 4, as follows:

```
HUMAN PROTEIN SEQUENCE (hCP41513)
MFRFPMGLLLGSVLLVASAPATLEPPGCSNKEQQVTVSHTYKIDVPKSALVQVDADPQPLSDDGASLLALGEAREEQNIIFRHN
```

[1]

This partial amino acid sequence of the Morris polypeptide is different from the amino acids 791 1054 of the polypeptide having the amino acid sequence show in SEQ ID NO: 4, shown below as follows:

```
Thr Asp Ile Asp Ser Pro Gln Asn Leu Val Thr
790                 795                 800
```

[1] This partial amino acid sequence is shown at pg. 119 of the text copy of the CD-ROM file.

```
Asp Trp Val Thr Glu Asn Thr Ala Thr Val Ser Trp Asp Pro Val Gln
                805                 810                 815

Ala Thr Ile Asp Arg Tyr Val Val His Tyr Thr Ser Ala Asn Gly Glu
            820                 825                 830

Thr Arg Glu Val Pro Val Gly Lys Glu Gln Ser Ser Thr Val Leu Thr
        835                 840                 845

Gly Leu Arg Pro Gly Met Glu Tyr Thr Val His Val Trp Ala Gln Lys
    850                 855                 860

Gly Asn Gln Glu Ser Lys Lys Ala Asp Thr Lys Ala Gln Thr Glu Ile
865                 870                 875                 880

Asp Gly Pro Lys Asn Leu Val Thr Asp Trp Val Thr Glu Asn Met Ala
                885                 890                 895

Thr Val Ser Trp Asp Pro Val Gln Ala Thr Ile Asp Lys Tyr Met Val
            900                 905                 910

Arg Tyr Thr Ser Ala Asp Gly Glu Thr Arg Glu Val Pro Val Gly Lys
        915                 920                 925

Glu His Ser Ser Thr Val Leu Thr Gly Leu Arg Pro Gly Met Glu Tyr
    930                 935                 940

Met Val His Val Trp Ala Gln Lys Gly Ala Gln Glu Ser Lys Lys Ala
945                 950                 955                 960

Asp Thr Lys Ala Gln Thr Glu Leu Asp Pro Pro Arg Asn Leu Arg Pro
                965                 970                 975

Ser Ala Val Thr Gln Ser Gly Gly Ile Leu Thr Trp Thr Pro Pro Ser
            980                 985                 990

Ala Gln Ile His Gly Tyr Ile Leu Thr Tyr Gln Phe Pro Asp Gly Thr
        995                 1000                1005

Val Lys Glu Met Gln Leu Gly Arg Glu Asp Gln Arg Phe Ala Leu Gln
    1010                1015                1020

Gly Leu Glu Gln Gly Ala Thr Tyr Pro Val Ser Leu Val Ala Phe Lys
1025                1030                1035                1040

Gly Gly Arg Arg Ser Arg Asn Val Ser Thr Thr Leu Ser Thr Val Gly
                1045                1050                1055
```

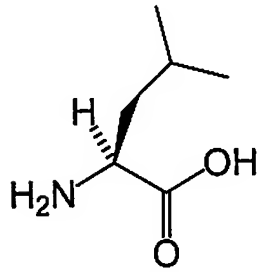
Therefore, the Morris reference cannot teach an "isolated antibody that specifically recognizes amino acids 791-1054 of the polypeptide having the amino acid sequence shown in SEQ ID NO: 4," as recited in the claims. Thus, the partial amino acid sequence disclosed by Morris fails to teach each and every limitation of the claimed sequence as Morris cannot teach an isolated antibody that specifically recognizes the *same* sequence.

Furthermore, the Examiner, although she made reference to a full-length sequence of SEQ ID NO: 2022 in the office action of 10/10/2008, failed to demonstrate that the sequence was available as of the filing date of March 1, 2002.

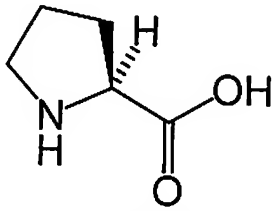
Arguendo, even if Morris disclosed the full-length sequence of SEQ ID NO: 2022 as of the filing date of March 1, 2002, Morris still fails to teach each and every limitation of the claimed sequence and therefore cannot teach an isolated antibody that specifically recognizes the sequence as claimed. The differences between the sequence alignment between the applicant's sequence (top) and Morris, referenced in the Office Action of 10/10/20008, are shown below:

```
Qy      901 DPVQATIDKYMVRYTSADGETREVPVGKEHSSTVLTGLRPGMEYMVHVWAQKGAQESKKA 960
            ||||||||||||||||||||||||| |||||||||| ||||||||||||||||||||||||
Db      901 DPVQATIDKYMVRYTSADGETREVLVGKEHSSTVLMGLRPGMEYMVHVWAQKGAQESKKA 960
```

Clearly, the Morris reference discloses two mismatches which cannot teach the limitations of the sequence disclosed by the Applicants. Instead, Morris discloses two mismatches, a natural amino acid, a Leucine at position 925, instead of a Proline, the only natural amino acid having secondary α-amino group, as disclosed in the sequence by the applicant, and a polar amino acid, Threonine at position 936 instead of a non-polar amino acid, Methionine. As it is well known in the art, small substitutions of amino acids have major consequences. A well-known clinical example, is sickle cell anemia, where one of the β-globin chains of hemoglobin has a glutamic acid substituted for a hydrophobic amino acid valine.[2] In the present case, the replacement of a Proline for a Leucine will have major consequences for the structure of the peptide. By contrast with Leucine, the distinctive cyclic structure of the proline's side chain locks its φ backbone dihedral angle at an angle of -75° and thus gives proline an exceptional conformational rigidity compared to other amino acids such as Leucine.[3] See comparison of the structure of Leucine vs. the structure of Proline:



Leucine



Proline

[2] Please see subsection "Genetics" of Wikipedia article entitled, "Sickle-cell disease," pg. 3.
[3] Please see attached references gathered from Wikipedia, particularly, pg. 6 of article entitled "Amino Acids," and subsection "Structural properties" of article entitled "Proline."

Thus, antibody specificity generated using the sequence disclosed by the Morris reference, will necessarily be different from an antibody generated by the sequence disclosed by the Applicants. Moreover, the second mutation replaces a polar amino acid, threonine, for a non-polar amino acid, methionine. Again, such a mutation will have major structural changes for a peptide. Additionally, the presence of two mutations in the middle portion of the peptide will have even more dramatic structural consequences. Therefore, the Morris reference fails to teach each and every limitation of the claims and cannot disclose an isolated antibody for the claimed sequence. Accordingly, Morris' antibody cannot possess the same structural and functional properties of the antibodies as claimed. Additionally, it is not obvious to replace a proline, the only natural amino acid having a secondary α-amino group, or substituting a polar amino acid for a non-polar amino acid, because such changes will have major structural consequences in the three-dimensional structure of the polypeptide, thereby affecting antibody binding affinity. Nor is it obvious to make two such amino acid substitutions, where such changes will have necessarily affect antibody binding affinity. Finally, Morris nowhere discloses one or more of the three C-terminal fibronectin III repeats of mammalian tenascin W and necessarily cannot teach an isolated antibody that would specifically recognizes these repeats. For all these reasons, the Applicants respectfully request the Examiner to withdraw the rejection under 35 U.S.C. § 102(e).

## CONCLUSION

Applicant respectfully submits that the claims are now in condition for allowance and notification to that effect is earnestly requested. This response is filed within the shortened statutory period of three months from the date of the mailing of the final office action, which response is due **August 6, 2009.** Therefore, it is believed no fees are required. Should this be incorrect, the Commissioner is authorized to charge any additional fees, or credit any overpayment, to deposit account No. 50-4255.

Should you wish to discuss the response further, please contact me or if I am not available, Brittany La.

Respectfully submitted,

Date July 6, 2009

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